

Evaluation of Cervical Cancer Detection Tests using Feature Ranking Aggregation

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Abstract— In the recent years, new tests for cervical cancer (CxCa) detection have emerged, aiming to replace Pap test or support diagnosis as ancillary tests. These techniques are either highly sensitive or highly specific, therefore none of them is superior over the others. Most of the published studies compare two tests against each other, while using different population study groups, thus it is questionable if their results can be used to perform a direct comparison between the CxCa tests available today. In this paper we present a sophisticated approach to directly compare several well known and widely applied CxCa tests, by employing a Feature Ranking Aggregation framework.

I. INTRODUCTION

In machine learning and statistics, Feature Ranking (FR) is the process of evaluating the significance of the individual features used to construct a model. FR algorithms use statistical and information theory measures in order to rank the individual features according to their importance to a target concept [1]. In this paper we adopt a FR framework in order to assess the importance of several medical tests available for the screening, triage and diagnosis of cervical cancer (CxCa).

II. MATERIALS AND METHODS

Anonymized data have been used, collected randomly from women enrolled in a study run by the Department of Cytopathology of ATTIKON University Hospital. The study was approved by the Bioethics Committee of the Hospital. From the patients' database, 740 cases with full tests' series were selected [2]. Each series included: (a) Pap test, (b) HPV DNA test that allows simultaneous detection of 35 different high or low risk HPV genotypes, (c) NASBA test for the identification of E6/E7 mRNA of the HPV types: 16, 18, 31, 33 and 45, (d) PermiFlow[®] test for the identification of E6/E7 mRNA expression of high-risk HPV using Flow Cytometry, and (e) immunocytochemical expression of protein p16 [2]. A cervical biopsy was performed if Pap test revealed cytological category ASCUS+ or there was a visible lesion during colposcopy. The histological diagnosis was used as the golden standard. The results of the HPV DNA test were expressed as

35 individual variables (either positive or negative); one for each HPV DNA genotype. For the NASBA test we used the result of each individual HPV type (16, 18, 31, 33 and 45). The result of the PermiFlow[®] test (FLOW) was used as positive or negative, as was the result of the p16 examination. Additionally, other variables expressing the HPV DNA test were included, for instance, the existence of high-risk (HR) or low-risk (LR) types was expressed as either positive or negative [2]. In total, a feature set consisting of 49 indicators deriving from the applied tests, was created. These indicators were evaluated on the basis of their efficacy in detecting high-grade cervical intraepithelial neoplasia or cancer (CIN2+) using 8 FR methods: Information Gain, Gain Ratio, Symmetric Uncertainty, Chi-Squared statistic, T-Test statistic, Area under ROC curve (AUC), mRMR algorithm, and ReliF algorithm [1, 2]. Each of these methods assesses the features using different measures, thus they produce different rankings. In order to produce a more robust ranking, we combined the different rank orderings using ranking aggregation [1]. For this purpose, we adopted the Schulze aggregation method (Schwartz Sequential Dropping), which, as shown in [1], leads to significantly better results than any other ranking method, either individual or aggregated.

III. RESULTS AND CONCLUSIONS

The 10 most significant features ranked according to their efficacy in detecting CIN2+ are: 1) Pap test, 2) FLOW, 3) NASBA (positive/negative), 4) p16, 5) HR HPV, 6) NASBA 16, 7) HPV DNA (positive/negative), 8) HPV 16, 9) NASBA 31 and, 10) NASBA 33. With regard to the importance of the HPV DNA types, these were ranked as follows: 1) HPV16, 2) HPV33, 3) HPV31, 4) HPV51, 5) HPV52, 6) HPV62, 7) HPV6, 8) HPV58, 9) HPV45, 10) HPV18. Several studies report that the CxCa tests are either highly sensitive or highly specific, and that a gain in sensitivity is at the expense of specificity and vice versa [2]. Thus, a direct comparison of these methods is difficult to be performed. Applying the proposed framework, we managed to directly compare and rank the most widely used CxCa tests. Such findings may guide pathologists in a step by step basis on which tests to perform following an abnormal Pap test, in order to decrease uncertainty, improve accuracy, and reduce diagnosis time and costs.

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